

Notice of Allowability

Application No.

10/764,853

Examiner

Anthony J. Paviglianiti

Applicant(s)

BIGOT ET AL.

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to Applicant's amendments dated April 18, 2005.
2. ☒ The allowed claim(s) is/are 2, 3, 4, and 6, now renumbered 1 - 4.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of the:
- ☒ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>20050512</u> . |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____. | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

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DETAILED ACTION

Claims 2 – 8 are currently pending in the application.

Response to Applicant's Remarks and Amendments

Applicant's remarks and amendments filed on April 18, 2005, are acknowledged.

An Examiner's Amendment to the record was agreed upon and authorized by Applicant on May 13, 2005.

The amendments have overcome the examiner's rejections to **Claims 2 – 8** brought under 35 U.S.C. §112, 1st paragraph, in the office action dated December 17, 2004. No new matter was found.

As the elected subject matter concerned "methods of use," **Claim 1** was not subject to rejoinder. **Claim 1** was cancelled by Applicant on May 13, 2005, and is deleted by Examiner's Amendment, as authorized by Applicant, below.

Examiner's Amendment

An examiner's amendment to the record appears below. Should the change be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

The following Examiner's Amendment was agreed to by the Examiner and Applicant, Irving Newman, Esq., and authorized by Applicant, on May 13, 2005:

In the amended claims (filed April 18, 2005):

Delete **Claim 1**.

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In **Claim 2**, page 3, lines 5 - 7, delete "A method of preventing excess NO production in a mammal in need of such prevention comprising administering to said mammal an effective i-NOS inhibiting amount of a compound of" and insert ---A method of inhibiting excess nitric oxide (NO) production in a mammal in need thereof to treat an illness selected from the group consisting of multiple sclerosis, cerebral, focal or global ischemia, cerebral or spinal trauma, Parkinson's disease, Huntington's disease, Alzheimer's disease, amyotrophic lateral sclerosis, migraine, depression, schizophrenia, anxiety and epilepsy, said method comprising administering to said mammal an effective inducible nitric oxide synthase (i-NOS) inhibiting amount of a compound of---

Delete **Claim 5**.

In **Claim 6**, page 4, line 15, delete "5" and insert ---2--- after the word claim.

Delete **Claim 7**.

Delete **Claim 8**.

In the Specification:

In the **Specification**, page 1, line 14, insert ---now U.S. Patent 6,699,867--- after the words November 8, 2002.

The above deletions and amendments are without prejudice for the applicant to pursue canceled claims to future applications, such as continuation or divisional applications.

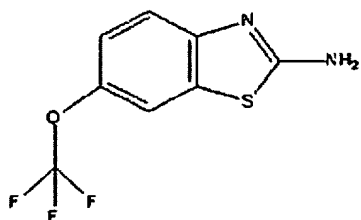
Reasons for Allowance

The present invention is directed to "methods of using" compounds or compositions of formula (I), as depicted in **Claim 2**, as inhibitors of excess nitric oxide production and inducible nitric oxide synthase for treatment of diseases selected from the group of multiple sclerosis,

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cerebral, focal or global ischemia, cerebral or spinal trauma, Parkinson's disease, Huntington's disease, Alzheimer's disease, amyotrophic lateral sclerosis, migraine, depression, schizophrenia, anxiety, and epilepsy. [The compounds and compositions of formula (I) of the present invention were previously issued a patent by this office in U.S. Patent No. 6,699,867 B2, issued March 2, 2004].

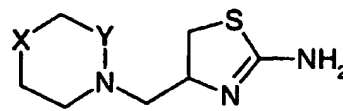
The closest prior art reported a method of using the pharmaceutical compound riluzole,



, to prolong survival in patients with amyotrophic lateral sclerosis.

Lacomblez, L. et al., "Dose-Ranging study of riluzole in amyotrophic lateral sclerosis," The Lancet, vol. 347(9013) pages 1425 – 1431 (May 25, 1996), at p. 1429, col. 2, lines 25 – 26 ("In this study, riluzole treatment of ALS had a positive and dose-dependent effect on tracheostomy-free survival"). Prior to this application, it was also shown in the art that riluzole possesses biological activity as an inhibitor of neuronal nitric oxide synthase (nNOS) activity in an experimental rat model. Keita, H., et al., "Anesthetic concentrations of riluzole inhibit neuronal nitric oxide synthase activity, but not expression, in the rat hippocampus," Brain Research, vol. 881, pages 237 – 240 (2000), at page 240, col. 1, lines 6 – 9 and 15 – 17 ("the fact that nNOS activity was inhibited both in vitro by riluzole and in rats anesthetized with this agent strongly supports physiological relevance of the reported effects...in summary, we have shown a concentration-related, competitive, inhibition of basal hippocampal nNOS activity by riluzole in

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the rat hippocampus'). The compounds of the present invention, , are related to riluzole in that each contains a "2-amino-thiazole" subunit in their chemical structure. The method of testing the degree of inhibitory activity against nitric oxide synthase (NOS) were nearly identical for the compounds of the present invention as compared with the inhibitory activity of riluzole against NOS. See Keita, et al., at p. 238, col. 1, lines 25 – 28 et seq. ("NOS activity was measured by the conversion of L-[³H] arginine to L-[³H] citrulline," etc.); compare Specification at page 10, lines 9 – 10. However, the prior art reference and the present invention are distinct because riluzole contains a condensed thiazole ring (i.e., a *benzothiazole* ring) which is not found in the present invention, and thus "methods of using" riluzole would not anticipate, nor render obvious, the claims for "methods of using" compounds of formula (I) of the present invention as inhibitors of excess nitric oxide (NO) production or inducible nitric oxide synthase (i-NOS) in the particular illnesses claimed.

Therefore, **Claims 2, 3, 4 and 6**, as amended by applicant and by Examiner's Amendment, are neither anticipated nor rendered obvious over the prior art of record, and are allowable.

Conclusion

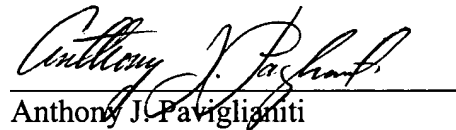
Claims 2, 3, 4 and 6, as amended by Examiner's Amendment, are allowed.

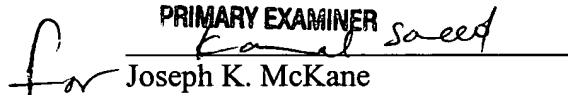
Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Anthony J. Paviglianiti** whose telephone number is (571) 272-3107. The examiner can normally be reached on Monday-Friday, 8:30 a.m. - 5:30 p.m.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached at (571) 272-0699. **The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300. Please note that this is a new central FAX number for all official correspondence.**

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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